Contains No CBI
FYHQ-92-12216
8892001038
INIT

RHÔNE-POULENC

RHÔNE-POULENC INC.
CN 7500, CRANBURY, NJ 08512-7500
TELEPHONE: (609) 860-4000

A

October 29, 1992

FEDERAL EXPRESS

Document Processing Center (TS-790)
Attn: Section 8(e) Coordinator (CAP Agreement)
Office of Toxic Substances
Environmental Protection Agency
401 M Street, S.W.
Washington, D.C. 20460

RE: Report Submitted Pursuant to the TSCA Section 8(e) Compliance Audit Program

CAP ID NO.: 8ECAP - 0004

RP CAP REPORT NO.: RPS - 0215

Dear Sir/Madam:

On behalf of Rhône-Poulenc Inc. (RPI, CN5266, Princeton, NJ 08543-5266) and its subsidiaries, the attached report is being submitted to the Environmental Protection Agency (EPA) pursuant to the Toxic Substances Control Act (TSCA) Section 8(e) Compliance Audit Program (CAP Agreement) executed by RPI and EPA (8ECAP - 0004).

The enclosed report provides information on the following chemical substance:

Product Name:	PX 073086 PX Solution Polymer
Identity:	1-Propanaminium, 2-hydroxy-N,N,N-trimethyl-3-[(2-methyl-1-oxo-2 propenyl)oxy]-nitrate(salt), polymer with 2-propenamide and 2-propenoic acid
CAS Registry No:	Unknown

4/4/93

The title of the enclosed report is:

Guinea Pig Maximization Test (Method of Magnusson and Kligman)

The following is a summary of the adverse effects observed in this report.

The test material exhibited a potential to produce dermal sensitization in the guinea pig. It was classified as a strong sensitizer (Grade IV).

RPI does not claim any portion of the information in this submission to be TSCA confidential business information (TSCA CBI).

RPI has not previously submitted any TSCA Section 8(e) notices on the subject chemical substance. A Premanufacturing Notification was submitted on October 25, 1985 (PMN P86-92).

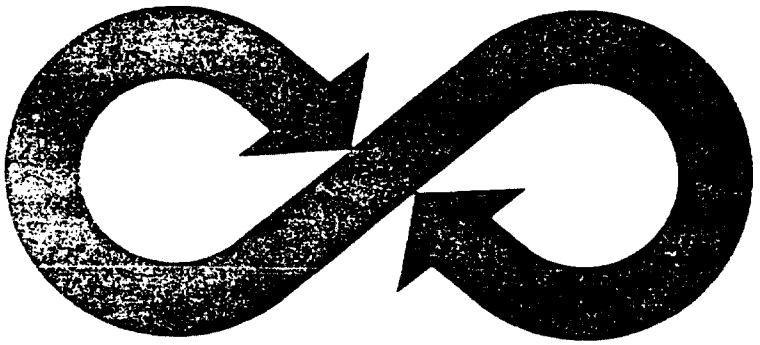
In total, RPI is submitting three copies of the enclosed report and this cover letter: an original and two copies.

Further questions regarding this submission may be directed to Dr. Glenn S. Simon, Director of Toxicology at (919)549-2222 (Rhône-Poulenc, P.O. Box 12014, 2 T.W. Alexander Drive, Research Triangle Park, NC 27709).

Sincerely,

Charles E. Moyer, Jr., Ph.D.
Director, Product Safety
(609)860-3589

CEMjr/mm
Enclosures



Bio/dynamics Inc.

Division of Biology and Safety Evaluation

BIO/DYNAMICS PROJECT NO.: 6837-86

ALLIED-SIGNAL PROTOCOL/PROJECT NO:86057/148C

FINAL REPORT FOR:

GUINEA PIG MAXIMIZATION TEST

(METHOD OF MAGNUSSON AND KLIGMAN)

TEST MATERIAL: PX 073086 (025-86B)

Submitted to: Allied-Signal, Inc.
Department of Toxicology
P.O. Box 1021R
Columbia Road
Morristown, New Jersey 07960

Attn: Brendan J. Dunn, M.S.

Date: November 9, 1987

TABLE OF CONTENTS

I. INTRODUCTION..... 1

II. EXPERIMENTAL DESIGN..... 1

III. DATES OF STUDY..... 1

IV. STUDY PERSONNEL..... 2

V. MATERIALS
A. Test and Control Materials..... 2
B. Test Animals..... 3

VI. METHODS
A. Route of Administration..... 4
B. Justification for Route of Administration..... 4
C. Doses..... 4
D. Preparation of Test and Control Materials..... 4
E. Preparation of Animals..... 4
F. Administration of Test and Control Materials..... 5

VII. EXPERIMENTAL EVALUATION..... 5

VIII. RAW DATA STORAGE..... 5

IX. RESULTS AND DISCUSSION..... 6

X. CONCLUSION..... 7

TABLES

Table I - Individual Body Weights..... 8
Table II - Individual Dermal Scores at Challenge..... 10

APPENDICES

Appendix A - Range-Finding Study - Individual Dermal Scores..... A-1
Appendix B - Acute Toxicology Protocol..... B-1
Appendix C - Letter or Authorization..... C-1
Appendix D - Compliance Statement..... D-1
Appendix E - Quality Assurance Statement..... E-1

I. INTRODUCTION

This study was conducted for Allied-Signal, Inc. in order to evaluate the allergic contact sensitization potential of PX 073086 (025-86B) in guinea pigs. This study was performed at Bio/dynamics, Inc., Mettlers Road, East Millstone, New Jersey 08873, using procedures based on the method described by Bertil Magnusson, M.D., and Albert M. Kligman, M.D. Ph.D. in "The Identification of Contact Allergens by Animal Assay. The Guinea Pig Maximization Test," Journal of Investigative Dermatology, 57, 268-276 and in Allergic Contact Dermatitis in the Guinea Pig. Identifications of Contact Allergens, Thomas, Springfield, Il., 1970.

This report has been reviewed by the Quality Assurance Unit of Bio/dynamics, Inc. to assure its conformance with the protocol and the raw data. All raw data and the original study protocol will be retained on file in the Bio/dynamics Archives.

II. EXPERIMENTAL DESIGN

Group	Test/Control Material	Number of Animals Females	Concentration (%) Induction Intradermal Site 1	Site 2	Site 3	Topical	Challenge	Rechalleng
IA[a]	DNCB (Positive Control)[a]	15	c	0.1[d]	0.1[e]	0.1[d]	0.1[d]	-
IB[a]	DNCB (Irritation Control)[a,b]	5	c	d	e	d	0.1[d]	-
IIA	PX 073086	15	c	5.0[f]	5.0[e]	100	100	100
IIB	PX 073086 (Irritation Control)[b]	5	c	f	e	g	100	-
IIC	PX 073086 (Irritation Control)[b]	5	c	f	e	g	-	100

[a]Positive control groups tested in this study were also used for Bio/dynamics Project No. 6803-86 (Allied-Signal Protocol No. 86037), which was run concurrently.
[b]Irritation control groups are treated with vehicle and/or FCA only, during Induction. Five animals serve as irritation controls for challenge and the other five for re-challenge (if necessary).
[c]Site 1 - animals received a 50% FCA/water emulsion.
[d]Vehicle: Propylene glycol.
[e]Site 3 - dose administered in a 50% FCA/water emulsion.
[f]Vehicle: Distilled water.
[g]Sham treated.

III. DATES OF STUDY

Animal Receipt: October 20, 1986

Range-Finding: October 28, 1986

III. DATES OF STUDY (cont.)

Induction of Sensitization -	
Intradermal:	Day 0: November 4, 1986
Topical:	Day 7: November 11, 1986
Challenge - Topical	Day 21: November 25, 1986
Evaluation of Response:	Days 23 and 24: November 27 and 28, 1986
Re-challenge:	Day 28: December 2, 1986
Evaluation of Response:	Days 30 and 31: December 4 and 5, 1986

IV. STUDY PERSONNEL

Study Director:	Donna L. Blaszcak, B.S., AALAS R.L.A.T.
Laboratory Supervisor:	Janet E. Trimmer, A.A.S., AALAS R.L.A.T.
Technician-in-Charge:	Mary Webb, B.S., AALAS R.L.A.T.

V. MATERIALS

A. Test and Control Materials:

1. Test Material: PX 073086 (025-86B)

Description:	Clear viscous liquid
Date of Receipt:	August 8, 1986
Received From:	Allied-Signal, Inc.
Storage:	Refrigerator (32°-46°F)
Vehicle:	Distilled water (Injection site 2)

2. Positive Control Material: 2,4-dinitrochlorobenzene (DNCB)

Lot Number:	A11E
Description:	Yellow granules
Supplier:	Eastman Kodak Company Rochester, New York
Storage:	Room temperature
Vehicle:	Propylene glycol (Injection site 2 and Topical applications)

V. MATERIALS (cont.)

A. Test and Control Materials (cont.):

3. Vehicle:	Propylene glycol
Lot Number:	336502
Description:	Clear viscous liquid
Supplier:	J.T. Baker Chemical Company Phillipsburg, New Jersey
Receipt Date:	January 9, 1984
Storage:	Room temperature
4. Adjuvant:	Freund's Complete Adjuvant (FCA)
Lot Number:	0638-60-7
Description:	A mixture of paraffin oil and an emulsifier with dead mycobacteria.
Supplier:	Difco Laboratories Detroit, Mich.
Receipt Date:	December 11, 1985
Storage:	Room temperature
5. Enhancer:	Sodium Lauryl Sulfate (SLS)
Lot Number:	110187
Description:	White powder
Supplier:	Aldrich Chemical Company Metuchen, New Jersey
Storage:	Room temperature

B. Test Animals:	Guinea Pigs
Stock:	Hartley Albino
Reason for Selection:	See Report Appendix B, page B-4.
Supplier:	Hazleton-Dutchland, Inc. Denver, Pennsylvania

V. MATERIALS (cont.)

B. Test Animals (cont.):

Number of Animals:	1. Range-finding: 8 females 2. Sensitization Study: 30 (two groups of fifteen females) 3. Irritation Controls: Challenge: 10 females (two groups of 5 females) Re-challenge: 5 females
Age:	3-4 weeks at receipt 5-6 weeks old at study initiation
Weight Range at Initiation of Treatment (Day 0):	304 to 399 grams
Equilibration Period:	Range-finding: 8 days Sensitization Study: 15 days
Husbandry:	See Report Appendix B, page B-5.
Animal Identification:	See Report Appendix B, page B-6.
Selection:	See Report Appendix B, page B-6.

VI. METHODS

A. Route of Administration: See Report Appendix B, page B-7.

B. Justification for Route of Administration: See Report Appendix B, page B-7.

C. Doses:

Prior to study initiation, a range-finding study was performed as described in Report Appendix B, page B-16 and Report Appendix A, page A-1. Based on results of the range-finding study (presented in Report Appendix A), the concentrations for the test material (as indicated in Section II Experimental Design) were selected by the sponsor.

VI. METHODS (cont.)

D. Preparation of Test and Control Materials:

1. Induction (Intradermal): See Report Appendix B, page B-8.

2. Induction (Topical): See Report Appendix B, page B-10.

3. Challenge (Topical): See Report Appendix B, page B-11.

4. Rechallenge (Topical): See Report Appendix B, page B-12.

E. Preparation of Animals:

1. Induction (Intradermal): See Report Appendix B, page B-8.

2. Induction (Topical): See Report Appendix B, page B-10.

3. Challenge (Topical): See Report Appendix B, page B-11.

4. Rechallenge (Topical): See Report Appendix B, page B-12.

F. Administration of Test and Control Materials:

1. Induction (Intradermal): See Report Appendix B, page B-9.

2. Induction (Topical): See Report Appendix B, page B-11.

3. Challenge (Topical): See Report Appendix B, page B-11.

4. Rechallenge (Topical): See Report Appendix B, page B-12.

VII. EXPERIMENTAL EVALUATION: See Report Appendix B, page B-12, B-17.

VIII. RAW DATA STORAGE

All raw data and the original study protocol and final report will be retained on file in the Bio/dynamics Archives.

IX. RESULTS AND DISCUSSION

A. Mortality:

All animals survived throughout the study.

B. Observations:

All animals appeared to be in good general health during the study.

C. Body Weights (Table I):

Most animals gained weight during the study. There was no evidence of an effect from PX 073086 administration.

D. Evaluation of Dermal Response (Table II):

Redness or edema at the challenge site at any of the observations which is greater than that seen in the irritation control animals is considered an allergic response. In general, dermal scores of 1 or greater (in the absence of dermal response in irritation control animals) are considered clearly indicative of sensitization. Scores of ± (barely perceptible erythema) are considered equivocal, although a high percentage of scores of ± in treated animals with no dermal response in irritation control animals is considered suggestive of sensitization. Number (percentages) of animals reacting, rather than intensity of reactions, is the criterion for categorizing materials as sensitizers and assessing sensitization potency (see Report Appendix B, page B-18).

All fifteen animals treated with DNCB (Group IA) exhibited dermal responses at challenge to a non-irritating concentration, as confirmed by a lack of a clear response by control animals (Group IB) to the same

IX. RESULTS AND DISCUSSION (cont.)

D. Evaluation of Dermal Response (cont.):

concentration. The 100% response categorizes this material as an Extreme Sensitizer (Grade V). This positive response to a known sensitizer demonstrates the susceptibility of this group of animals to sensitization in the guinea pig maximization test and validates the test procedure used to evaluate PX 073086 (025-86B).

Because only four of the fifteen animals (27%) challenged with PX 073086 (025-86B), Group IIA, exhibited clear dermal responses (scores of 1 or greater) at challenge, a second challenge was performed at the request of the sponsor. Eleven of the fifteen animals (73%) re-challenged exhibited clear dermal responses.

No significant dermal response occurred in irritation control animals (Group IIB at Challenge; Group IIC at Re-challenge).

X. CONCLUSION

Under conditions of this study, PX 073086 (025-86B) exhibited a potential to produce dermal sensitization in the guinea pig and is categorized as a Strong (Grade IV) Sensitizer (as defined in Report Appendix B, page B-18).

Donna L Blaszcak 11/4/87

Donna Blaszcak, B.S., AALAS R.L.A.T. Date
Study Director
Manager, Acute Toxicology

Carol A. Auletta 11/9/87

Carol Auletta, B.A., D.A.B.T. Date
Associate Director of Toxicology

TABLE I

FINAL REPORT FOR:

GUINEA PIG MAXIMIZATION TEST WITH PX 073086 (025-86B)

INDIVIDUAL BODY WEIGHTS (GRAMS)

Animals Treated at Induction and Challenge

	Animal No. And Sex	-7	0	7	14	21	28
Group IA DNCB	8373 F	290	334	363	384	432	-
	8350 F	301	340	364	379	446	-
	8380 F	332	364	394	419	477	-
	8336 F	312	368	401	434	504	-
	8331 F	271	320	355	380	423	-
	8383 F	287	334	376	420	474	-
	8377 F	302	351	380	408	439	-
	8356 F	316	361	380	394	423	-
	8418 F	276	320	366	406	476	-
	8361 F	307	340	385	422	478	-
	8407 F	300	339	368	408	457	-
	8342 F	292	327	342	353	410	-
	8408 F	267	306	325	351	417	-
	8338 F	311	366	406	430	489	-
	8385 F	318	366	397	409	476	-
	Mean	299	342	373	400	455	
	S.D.	18	20	22	26	30	
Group IIA PX 073086	8332 F	309	349	366	388	415	437
	8390 F	279	315	347	389	422	447
	8357 F	332	376	382	425	464	475
	8334 F	292	332	357	384	440	443
	8335 F	293	334	346	370	421	451
	8379 F	319	366	385	419	470	478
	8416 F	288	346	345	403	448	482
	8359 F	305	356	378	418	492	482
	8347 F	298	356	381	402	470	474
	8355 F	277	329	354	393	442	452
	8344 F	313	356	386	438	512	555
	8396 F	299	357	377	392	448	459
	8402 F	322	375	413	430	483	490
	8360 F	264	322	357	394	472	506
	8333 F	293	334	361	395	449	474
	Mean	299	347	369	403	457	474
	S.D.	18	19	19	19	27	30

TABLE I (cont.)

FINAL REPORT FOR:

GUINEA PIG MAXIMIZATION TEST WITH PX 073086 (025-86B)

INDIVIDUAL BODY WEIGHTS (GRAMS)

IRRITATION CONTROL ANIMALS

	Animal No. And Sex	-7	0	7	14	21	28
Group IB DNCB	8372 F	304	361	390	393	459	-
	8364 F	285	324	360	385	432	-
	8394 F	309	363	415	461	521	-
	8393 F	278	315	323	339	382	-
	8419 F	327	366	373	385	431	-
	Mean	301	346	372	393	445	
	S.D.	20	24	34	44	51	
Group IIB PX 073086	8398 F	264	304	318	343	378	-
	8369 F	333	387	407	422	477	-
	8349 F	281	339	396	400	484	-
	8341 F	305	353	370	379	462	-
	8392 F	312	353	368	410	469	-
	Mean	299	347	372	391	454	
	S.D.	27	30	34	31	43	
Group IIC PX 073086	8397 F	329	399	432	422	522	588
	8386 F	301	349	373	428	493	543
	8399 F	310	360	392	400	455	514
	8340 F	292	342	364	407	453	525
	8405 F	274	312	321	353	399	441
	Mean	301	352	376	402	464	522
	S.D.	20	32	41	30	46	53

TABLE II

FINAL REPORT FOR:

GUINEA PIG MAXIMIZATION TEST WITH PX 073086 (025-86B)

INDIVIDUAL DERMAL SCORES[a] AT CHALLENGE

GROUP I: 0.1% DNCB

Group IA (Animals Treated During Induction)					Group IB (Irritation Control Animals)				
Animal No. and Sex	Test Site 24 Hr	Test Site 48 Hr	Control Site 24 Hr	Control Site 48 Hr	Animal No. and Sex	Test Site 24 Hr	Test Site 48 Hr	Control Site 24 Hr	Control Site 48 Hr
8373 F	2	1	0	0	8372 F	0	±	0	0
8350 F	2	2	0	0	8364 F	0	0	0	0
8380 F	1	2	0	0	8394 F	0	0	0	0
8336 F	2	2	0	0	8393 F	0	0	0	0
8331 F	2	2	0	0	8419 F	0	0	0	0
8383 F	2	2,Ed	0	0					
8377 F	2	2,Ed	0	0					
8356 F	2	2	0	0					
8418 F	2	2,Ed	0	0					
8361 F	1	2	0	0					
8407 F	2	2,Ed	0	0					
8342 F	2	2	0	0					
8408 F	2,Ed	2	0	0					
8338 F	1	2	0	0					
8385 F	1	2	0	0					

[a]Scored using scale presented in Report Appendix B, page B-17.
F=Female; Ed=Edema

TABLE II (cont.)

FINAL REPORT FOR:

GUINEA PIG MAXIMIZATION TEST WITH PX 073086 (025-86B)

INDIVIDUAL DERMAL SCORES[a] AT CHALLENGE

GROUP II: PX 073086 (100%)

Group IIA (Animals Treated During Induction)						
	Challenge				Re-Challenge	
Animal No. and Sex	Test Site		Control Site			
	24 Hr	48 Hr	24 Hr	48 Hr	24 Hours	48 Hours
8332 F	0	0	0	0	0	0
8390 F	0	0	0	0	1	±
8357 F	1	±	0	0	1	±
8334 F	±	0	0	0	1	1
8335 F	0	±	0	0	0	0
8379 F	0	±	0	0	1	±
8416 F	1	1	0	0	1	1
8359 F	1	±	0	0	2	1
8347 F	0	±	0	0	0	0
8355 F	±	±	0	0	1	±
8344 F	0	0	0	0	0	0
8396 F	0	0	0	0	1	±
8402 F	±	1	0	0	2,Ed	1
8360 F	±	±	0	0	1	±
8333 F	±	±	0	0	1	±

[a]Scored using scale presented in Report Appendix B, page B-17.
F=Female; Ed=Edema

TABLE II (cont.)

FINAL REPORT FOR:

GUINEA PIG MAXIMIZATION TEST WITH PX 073086 (025-86B)

INDIVIDUAL DERMAL SCORES[a] AT CHALLENGE

GROUP II: PX 073086 (100%)

Irritation Control Animals

Challenge (Group IIB)					Re-Challenge (Group IIC)		
Animal No. and Sex	Test Site		Control Site		Animal No. and Sex	24 Hour	48 Hour
	24 Hr	48 Hr	24 Hr	48 Hr			
8398 F	0	0	0	0	8397 F	0	0
8369 F	0	0	0	0	8386 F	0	0
8349 F	0	0	0	0	8399 F	0	0
8341 F	0	0	0	0	8340 F	0	0
8392 F	0	0	±	0	8405 F	0	0

[a]Scored using scale presented in Report Appendix B, page B-17.
F=Female

REPORT APPENDIX A

RANGE-FINDING STUDY - INDIVIDUAL EVALUATIONS

BIO/DYNAMICS PROJECT NO.: 6837-86

FINAL REPORT FOR:

GUINEA PIG MAXIMIZATION TEST WITH PX 073086 (025-86B)

APPENDIX A

FINAL REPORT FOR:

GUINEA PIG MAXIMIZATION TEST WITH PX 073086

RANGE-FINDING STUDY - INDIVIDUAL EVALUATIONS

INTRADERMAL INJECTIONS:[a]

Animal No. and Sex	5%[c]				3%[c]				1%[c]			
	Site #1		Site #2		Site #3		Site #4		Site #5		Site #6	
	24 Hr	48 Hr	24 Hr	48 Hr	24 Hr	48 Hr	24 Hr	48 Hr	24 Hr	48 Hr	24 Hr	48
8315 F	N+	N+	N+	N+	0	0	0	0	N+	0	N+	0
8316 F	N+	N+	N+	N+	N+	N+	N+	N+	N+	N+	N+	N+

TOPICAL APPLICATION:[b]

Animal No. and Sex	Concentration							
	100%		50%[c]		25%[c]		10%[c]	
	24 Hr	48 Hr	24 Hr	48 Hr	24 Hr	48 Hr	24 Hr	48 Hr
8309 F	0	0	0	0	0	0	0	0
8310 F	0	0	0	0	0	0	0	0
8311 F	0	0	0	0	0	0	0	0
8312 F	0	0	0	0	0	0	0	0
8313 F	0	0	0	0	0	0	0	0
8314 F	0	0	0	0	0	0	0	0

[a]Observed for necrosis and ulceration only:
0=No necrosis or ulceration
N+=Local necrosis (acceptable)
N++=Extensive necrosis (not acceptable)
U=Ulceration (not acceptable)
[b]Scored according to scale presented in Report Appendix B, page B-17.
[c]Vehicle: distilled water.
F=Female

REPORT APPENDIX B

STUDY PROTOCOL*

BIO/DYNAMICS PROJECT NO.: 6837-86

FINAL REPORT FOR:

GUINEA PIG MAXIMIZATION TEST WITH PX 073086 (025-86B)

---

* The Sponsor authorization letters (pages 15 and 20) were moved to Report Appendix C.

Approved by: D L Blaszcak

Date: 10/24/86

Date of Distribution: 10/24/86

Original to: DLK

Copies to: JET
QA

ACUTE TOXICOLOGY PROTOCOL

Project No.: 6837-86 A-1

Study: GUINEA PIG MAXIMIZATION TEST WITH PX 073086

Study Director: Donna L. Blaszcak

Time spent on this study should be assigned to account number: 0116

Protocol Changes:

No.	Page No.	Approved by	Date	Date of Distribution
11-4-86 1	17, 20	D L Blaszcak	11/12/86	✓ 11/13/86
		✓		

I. INTRODUCTION

A. PROJECT NO.: 6837-86

B. TEST MATERIAL: ALD-SGN# PX 073086 (025-86B)

C. SPONSOR CODE: A-1

D. STUDY: Guinea Pig Maximization Test (Method of Magnusson and Kligman)

E. BIO/DYNAMICS PROTOCOL NO.: A-1/GP/MT

ISSUE NUMBER AND DATE: ISSUE 1 AUGUST 1986

SPONSOR PROTOCOL NO.: 86057

F. PURPOSE: This study is designed to evaluate the allergic contact sensitization potential of the test material(s) in guinea pigs.

G. STUDY DESIGN REFERENCE:

The method employed is that described by: Bertin Magnusson, M.D. and Albert M. Kligman, M.D., Ph.D. in "The Identification of Contact Allergens by Animal Assay. The Guinea Pig Maximization Test", Journal of Investigative Dermatology, 57, 268-276 and in Allergic Contact Dermatitis in the Guinea Pig. Identifications of Contact Allergens, Thomas, Springfield, Il., 1970.

H. TESTING FACILITY: Bio/dynamics Inc.
P.O. Box 43
Mettlers Road
East Millstone, New Jersey 08873

I. SPONSOR: Allied-Signal Inc.
Department of Toxicology
P.O. Box 1021R
Columbia Road
Morristown, New Jersey 07960

J. DATE OF AUTHORIZATION: 8/8/86

K. PROPOSED STUDY DATES: Animal Receipt: 10/20/86
Range-Finding: 10/27/86 (week 1)
First Induction: 11/4/86
Challenge: 11/25/86
Termination: 48 hours after last challenge

I. INTRODUCTION (cont.)

L. STUDY PERSONNEL

Study Director: DONNA L. BLASZCAK
Supervisor: JANET E. TRIMMER
Technician-In-Charge: MARY WEBB

M. STUDY CONDUCT:

This study will be conducted following EPA-TSCA Good Laboratory Practices (Part 792 of 40 CFR). All amendments or deviations to the protocol will be approved in writing by the sponsor.

II. EXPERIMENTAL DESIGN

Group	No. of Animals females	Concentration					
		Induction					Re-
		Intradermal			Topical	Challenge	challe
		Site 1	Site 2	Site 3			
DNCB Positive Control	15	c	0.1%[d]	0.1%[e]	0.1%[d]	0.1%[d]	none
DNCB Irritation Control[a]	5	c	d	e	d	0.1%[d]	none
Test Material[b]	15	c	5%[d,f]	5%[e,f]	g,i	h,i	h,i
Test Material Irritation Control[a]	5	c	d	e	i	h,i	none
Test Material Irritation Control	5	c	d	e	i	i	h,i

[a]Irritation control groups are treated with vehicle and/or FCA only, during Induction. Five animals serve as irritation controls for challenge and the other five for re-challenge (if necessary).
[b]More than one test material may be tested concurrently with the same positive control group.
[c]50% FCA/water emulsion.
[d]Vehicle: propylene glycol.
[e]Administered in a 50% FCA/water emulsion.
[f]5% or highest level which can be tolerated locally and generally.
[g]Minimal irritant concentration; 100% if non-irritating (See IVE).
[h]Maximum non-irritant concentration (See IVE).
[i]Vehicle to be determined by sponsor.

III. MATERIALS

A. Test Material: PX 073086

Handling Information: As described in Appendix A. Unless otherwise noted, the identity, strength, purity, composition, stability and method of synthesis, fabrication and/or derivation of the test materials(s) will be documented by the sponsor.

B. Positive Control: Dinitrochlorobenzene (DNCB).

C. Vehicle:

DNCB: The vehicle for DNCB will be propylene glycol.

Test Material(s): The vehicle for the test material(s) will be determined by the sponsor.

D. Positive Control: Dinitrochlorobenzene (DNCB).

E. Adjuvant: Freund's Complete Adjuvant (FCA) (A mixture of paraffin oil and an emulsifier with mycobacteria). Difco Laboratories, Detroit, Mich.

F. Enhancer: Sodium Lauryl Sulfate (SLS)

G. Test Animals: Albino guinea pigs

1. Stock: Hartley

a. Reason for Selection: Standard laboratory animal for dermal sensitization studies. The Hartley Albino breed is used because of its availability and because of the existing historical data base for comparative evaluation.

Although the TSCA test rules suggest the use of male guinea pigs, the female sex is preferred because of the historical data base with females. [Note: Previous work by the sponsor was performed with group housed animals and since the aggressive social behavior of males may have resulted in considerable skin damage that might have interfered with the interpretation of challenge reactions, females were used].

b. Supplier: Hazleton Dutchland, Inc.
Denver, Pennsylvania
or other acceptable supplier

III. MATERIALS (cont.)

G. Test Animals:

2. Number and Sex: Range-finding:

8 females (or as indicated by experimental findings)

DNCB:

15 females for the postive control group and 5 females per irritation control group*

Test Material(s):

15 females per test material group and 10 females per test material for irritation control groups (5 for challenge, 5 for re-challenge).*

*See Experimental Design

3. Age: 3-4 weeks at receipt
5-6 weeks old at study initiation

4. Weight: Approximately 200-250 grams at receipt
Approximately 250-500 grams at initiation of study

5. Equilibration Period: Range-finding: at least one week.
Sensitization Study: at least two weeks

Observations: All animals will be checked for viability twice daily. Prior to assignment to study all animals will receive a physical examination to ascertain suitability for study.

6. Husbandry: Currently acceptable practices of good animal husbandry will be followed, e.g., Guide for the Care and Use of Laboratory Animals; NIH Publication No. 85-23 Revised 1985.

a. Housing: Individually housed

b. Cages: Suspended, stainless steel with wire mesh bottoms. Racks will be cleaned at least three times per week.

III. MATERIALS (cont.)

G. Test Animals (cont.)

6. Husbandry (cont.):

c. Environmental Conditions:

1. Temperature: 65-75°F is considered an acceptable temperature range for guinea pigs; room temperature will be monitored twice daily and maintained within this range to the maximum extent possible.

2. Humidity: 40-70% is considered an acceptable humidity range for guinea pigs; room humidity will be monitored and recorded daily and maintained within this range to the maximum extent possible.

3. Light Cycle: 12 hours light, 12 hours dark (controlled by an automatic timer).

d. Food: Agway Prolabs - Guinea Pig diet or acceptable substitute, ad libitum.

e. Water: Automatic watering system, ad libitum, Municipal water supply (Elizabethtown Water Co.). Monthly water analyses, performed by Elizabethtown Water Co., are kept on file.

f. Contaminants: There are no known contaminants reasonably expected to be found in food or water which would interfere with the results of this study.

7. Identification: Each animal will be identified with a monel ear tag, bearing a unique number, prior to testing.

8. Selection: Approximately 20% more animals than required will be obtained for the study. Any animals considered unsuitable because of poor health, outlying body weights or unacceptable skin will be excluded. Animals considered suitable for study will be randomized by body weight (Day -7 body weights), using analysis of variance, into control and/or treated groups. All animals will be from the same shipment.

IV. METHODS

A. Route of Administration:

Induction: Intradermal injection, in the clipped shoulder region.
Topical application, on the clipped shoulder region.

Challenge(s): Topical application, on the clipped skin of the flanks.

B. Justification for Route of Administration:

The study was intended to provide information on the health hazards likely to arise from exposure to the test material by the dermal route; skin contact is a possible worker and consumer exposure route. The guinea pig maximization test is an acceptable method for evaluating the potential of test materials to produce dermal sensitization.

C. Duration of Study:

4-5 weeks

D. Schedule:

This test consists of two segments, 1) attempted induction of sensitization and 2) challenge of animals to evaluate presence and/or extent of sensitization. The following summary describes the sequence of steps. Detailed information is presented below.

Day 0	- Induction of sensitization by intradermal injection
Day 7	- Induction of sensitization by topical administration
Day 21	- Challenge by topical administration
Days 23 & 24	- Evaluation of response
Day 28	- Re-challenge by topical administration (if required)
Day 30 & 31	- Evaluation of response

E. Doses:

Prior to initation of the study, a range-finding study will be performed as described in Appendix B. Based on this study, the sponsor will select doses as follows:

IV. METHODS (cont.)

E. Doses (cont.):

1. Induction (Sites 2 and 3):

a. Intradermal:

The test material will be administered at a concentration of 5%, provided that the injection does not produce significant local or systemic toxicity. Otherwise the concentration will be adjusted to the highest level that can be well-tolerated locally and generally; this will usually fall within the 1-5% range and will be determined by a preliminary range-finding study, if indicated.

b. Topical Application:

Minimal irritant concentration (the lowest concentration which produces some irritation, i.e., scores of 1 or higher in one or more animals). Non-irritating materials will be administered at 100% concentration.

2. Challenge:

Maximum non-irritant concentration (the highest concentration which does not produce scores of 1 or higher in any animal and which produces scores of ± in less than half of the animals.) This concentration will be applied at challenge to animals treated during the induction phase and to animals which have only been treated with FCA and vehicle (irritation control groups).

F. Induction Procedures:

1. Day 0 - (Intradermal Injections):

a. Preparation of Animals:

The hair in the shoulder region (approximately 4 x 6 cm) will be clipped short with an electric clipper (using a No. 40 blade).

b. Preparation of Test/Control Materials:

1) Site 1: FCA/Water Emulsion:

Prior to injection an emulsion will be prepared by blending the commercial adjuvant with an equal volume of deionized water.

IV. METHODS (cont.)

F. Induction Procedures (cont.):

1. Day 0 (Intradermal Injections) (cont.):

b. Preparation of Test/Control Materials (cont.):

2) Site 2: Test/Control Material in Vehicle:

Appropriate amounts of test/control material and vehicle will be mixed to achieve the desired concentration.

3) Site 3: Test/Control Material in FCA:

The adjuvant will be placed in a container, the aqueous phase will be added and the emulsion mixed until a homogeneous mixture is obtained. Water-soluble substances will be dissolved in the aqueous phase prior to blending. Oil-soluble substances will be dissolved or suspended in the adjuvant prior to blending with the aqueous phase.

c. Administration:

Substances will be administered by intradermal injection, using a 1.0 cc syringe and a 25 or 26 gauge needle, in the clipped shoulder area (larger-gauge needles will be used for test material injections if necessitated by the nature of the test material). A row of three injections will be made on each side, for a total of six injections, as diagrammed. Injections 1 and 2 will be given close together and nearest to the head; injection 3, most caudally. The injections will consist of the following:

No. 1 - 0.1 ml of FCA/water emulsion without test substance

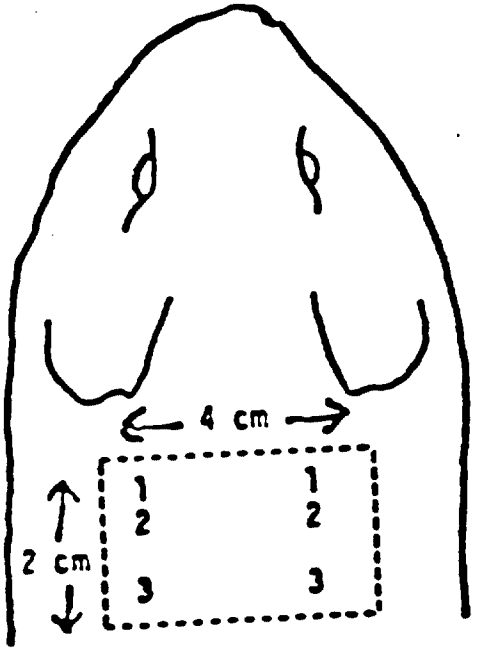
No. 2 - 0.1 ml of test or control substance in an appropriate vehicle (propylene glycol if possible).

No. 3 - 0.1 ml of test or control substance/FCA emulsion.

The injections will be made within the boundaries of the 2x4 cm area over which a patch is applied the following week. [Note: Irritation control animals will receive FCA and/or vehicle only].

IV. METHODS (cont.)

F. Induction Procedures (cont.):



2. Day 7 - (Topical Application):

a. Preparation of Animals:

The hair will be clipped from the 4x6 cm area treated previously. If the test substance is non-irritating, the area will be pretreated with 10% sodium lauryl sulfate (SLS) in petrolatum on the day before the test patch is applied in order to provoke a mild inflammatory reaction. (The SLS will be massaged into the skin with gloved fingers).

b. Preparation of Test and Control Materials:

Liquids will be used as received or diluted with an appropriate vehicle. Powders will be dissolved or suspended in an appropriate vehicle. Particulates will be ground using a mortar and pestle and then dissolved or suspended in an appropriate vehicle.

IV. METHODS (cont.)

F. Induction Procedures (cont.):

2. Day 7 - (Topical Application) (cont.):

c. Administration of Test and Control Materials:

If the test substance is mixed in petrolatum, it will be spread over a 2 x 4 cm filter paper in a thick even layer; liquids will be applied to the filter paper to saturation (volume will be recorded). The filter paper will then be covered by overlapping, impermeable plastic and this will be firmly secured by an elastic adhesive bandage which is wound around the torso of the animal. The vehicle, without the test substance, and the positive control material will be applied to control animals in the same manner as the test substance. [Note: the irritation control animals will receive vehicle only]. The patches will be left in place for 48 hours after which they will be removed and the skin wiped free of any excess material. If there is severe irritation at the dose site, petrolatum will be applied at the site to help relieve the trauma.

G. Challenge Procedures:

1. Day 21 - (Challenge):

a. Preparation of Animals:

The hair will be removed from a 5x5 cm area on both flanks by clipping as described previously.

b. Preparation of Test and Control Materials:

Liquids will be used as received or diluted with an appropriate vehicle. Powders will be dissolved or suspended in an appropriate vehicle. Particulates will be ground using a mortar and pestle and then dissolved or suspended in an appropriate vehicle.

c. Administration of Test and Control Substances:

Patches will be applied to the flanks using the same procedur as for topical application on Day 7, except that a 2x2 cm piece of filter paper will be used and allowed to remain on the animal for 24 hours. The test or control material will be applied to the left flank and vehicle will be applied to the right flank. The irritation control animals (5 animals per material) will be treated in the same manner as the test animals.

IV. METHODS (cont.)

G. Challenge Procedures (cont.):

2. Day 28 - Re-challenge (if required):

If the responses are clearly positive, no re-challenge is necessary and the study is terminated.

If reactions are negative or equivocal, the sponsor will be consulted, and, if requested, a second challenge will be performed approximately one week after the initial challenge, using a second group of 5 animals for irritation controls. The same procedures as used for challenge will be followed except only the right flanks will be dosed. The left flanks will not be dosed. Either the same concentration or a new concentration (higher or lower) of test material may be used, depending on the result of the first challenge.

V. EXPERIMENTAL EVALUATION

A. Viability Check:

Twice Daily

B. Observations:

Animals will be observed prior to treatment and weekly during the study for general health; unusual observations will be recorded. (Animals which are not considered to be in good health prior to treatment will not be placed on study).

C. Body Weights:

Animals will be weighed on Days -7 (weights used for randomization), 0 (day of 1st induction), 7, 14, 21 and 28.

D. Evaluation of Dermal Response:

1. Intervals:

Readings will be made on all animals 24 and 48 hours after the removal of the patches at challenge. (The challenge area will be gently clipped after the 24 hour observation).

2. Methods:

Reactions will be scored according to the system in Appendix C.

VI. POST-MORTEM

A gross necropsy will be performed on any animal which dies spontaneously. Abnormal observations will be recorded but no tissues will be saved. Postmortem examinations will not be performed on animals which survive throughout the study.

VII. ALLERGENICITY RATING

Redness at the challenge site which is clearly greater than that seen in the irritation control animals is considered an allergic response. In general, dermal scores of 1 or greater (in the absence of dermal response in irritation control animals) are considered clearly indicative of sensitization. Scores of ± (barely perceptible erythema) are considered equivocal, although a high percentage of scores of ± in treated animals with no dermal response in irritation control animals is considered suggestive of sensitization. Number (percentages) of animals reacting, rather than intensity of reactions, is the criterion for categorizing materials as sensitizers and assessing sensitization potency.

Sensitizers are categorized, based on percentage of animals affected, as weak (Grade I) to extreme (Grade V) sensitizers. (See Appendix D).

VIII. CONTROL CRITERIA FOR A VALID TEST SYSTEM

A positive response to DNCB in at least 70% of the animals in the positive control group, will demonstrate the susceptibility of this group of animals to sensitization. If less than 70% of these animals respond the test will be repeated.

IX. RAW DATA

Data for all parameters outlined above will be recorded and retained permanently, with the original study protocol, on file in the Bio/dynamics Archives.

X. TEST MATERIAL RETURN

An archival sample will be obtained at the time of the last dose preparation of the last scheduled study involving this test material. The sample will be measured (2 g for solids; 2 ml for liquids), placed in a scintillation vial (preferably plastic, otherwise glass) or other appropriate container, sealed, labelled and returned to the sponsor.

After completion of the study and submission of the final report, all unused samples of the test material(s) will be returned to the sponsor, using labels and shipping instructions provided by the sponsor.

XI. REPORT

One copy of the draft report will be sent to the sponsor for approval following the termination of the study. Five copies of the approved final report will then be submitted to the sponsor. (Additional copies will be at additional cost). The report will contain the following:

- Narrative discussion of study results
- Table of individual and mean body weights
- Table of individual dermal scores
- Summary table of dermal scores
- Study protocol
- Copy of sponsor authorization to conduct the study

XII. QUALITY ASSURANCE

Each study will be subjected to a final report audit by Quality Assurance personnel. In addition, studies will be randomly selected for procedure audits. The subject of the procedure audit will be randomly selected from the following list:

- Protocol Generation/Documentation
- Prestudy Preparation
- Test and/or Control Material Preparation
- Test and/or Control Material Determination
- Periodic Measurements/Assessments
- Facilities - Personnel
- Necropsy - Animal Termination

XIII. PROTOCOL REVIEW AND ACCEPTED

BY: Dana L Blaszak Date: 8/18/86
For: Bio/dynamics, Inc.

BY: Brendan J. Dunn Date: 8/19/86
For: Allied-Signal Inc.

APPENDIX A
TEST AND/OR CONTROL MATERIAL
HANDLING INFORMATION

PROJECT NO(S): MA-148C 6837-86

Test: Guinea Pig Maximization 16 6420

This form is designed to specify test material handling and disposition instructions and to provide procedures (if known) in case of accidental exposure to the substance. As with all data, this information will be considered confidential and will be available only to persons involved with the study or studies using this substance. Please provide as complete information as possible for each category below and/or attach the information in your own form and return to Study Director of your study at Bio/dynamics, Inc., Box 43, E. Millstone, N.J. 08873. Bio/dynamics Protocol No.: A-1/GP/MT
Sponsor Protocol No.: 86057

I. IDENTIFICATION

TEST MATERIAL (Name or Code Number) PX 073086 (025-86B)

BATCH OR LOT NO.: Not Applicable (NA)

PHYSICAL DESCRIPTION: Clear viscous liquid

PURITY: 5% in water

DENSITY (IF KNOWN):* unknown

TEST MATERIAL IS SOLUBLE IN (CHECK ONE) WATER X; ACETONE ____; ALCOHOL ____; OIL ____; OTHER ____

II. STORAGE INFORMATION

MATERIAL SHOULD BE STORED IN:

____ Temperature-monitored room (60°-85°F); ____ Freezer

X Refrigerator ____ Other ____

III. STABILITY

LENGTH OF TIME MATERIAL IS STABLE UNDER CONDITIONS DESCRIBED ABOVE: Assumed stable for duration test under conditions of st

EXPIRATION DATE: DATE: unknown INDICATED ON LABEL: YES (NO) (circle one)

STABILITY IN COMMON VEHICLES:	Unknown	Less than 4 hours	Up to 4 hours	Up to 24 hours	Other (Specify)
WATER				X	
METHYCELLULOSE					
CORN OIL					
ORGANIC SOLVENTS (ACETONE, ETHANOL)					
OTHER (SPECIFY: ____)					

If stability of neat material or of material in vehicle to be used in study is unknown:

____ Instructions for analysis will be provided

____ Samples are to be submitted to sponsor ~~for analysis~~ X Analysis will not be required

IV. HANDLING (EMPLOYEE SAFETY) INFORMATION

KNOWN HAZARDS: (if available, attach summary of pertinent results of any previous toxicity studies).

Approximate rodent oral LD_{50} = >10 mL /kg (if unavailable, enter NK, not known)

Is material a probable eye/skin irritant? (yes) no

OTHER PERTINENT INFORMATION: ____

PRECAUTIONS: Use of protective clothing (laboratory coats), latex gloves, safety glasses and dust mask is routine. Precautions in excess of the above should be specified:

X Routine precautions adequate. Other ____

IN CASE OF EMERGENCY RELATED TO THIS SUBSTANCE, CONTACT:

Gordon Loewengart, Ph.D. (Person) of Allied-Signal Inc. (Company) at (201)455-338 (Phone #)

V. DISPOSITION

All materials will be returned to the sponsor. Person and address to whom samples are to be returned:

Name: Gordon Loewengart, Ph.D.

Address: Dept. of Toxicology
Allied-Signal Inc.
Columbia Rd., Morristown, N.J. 07960

Shipping Instruction: ____

NOTE: PLEASE ENCLOSE APPROPRIATE SHIPPING LABELS FOR RETURN

VI. SIGNATURE

Information submitted by: [signature]

~~16 of 18~~ 17 ~~19~~ 20

6837-8

(1) See page 20

APPENDIX B

Guinea Pig Maximization Test - Range-Finding Study

1. Topical:

In order to evaluate the topical irritation potential of the test material, six animals per test substance will be subjected to preliminary studies as follows:

Animals will be closely clipped over the back and sides with an electric clipper. The Sponsor, Study Director, or Laboratory Supervisor will decide upon four different test material concentrations, based on knowledge of the test material. If there is no information on the suspected irritancy, the following concentrations will be used: 100%, 50%, 25%, and 10%. The vehicle commonly used is 70% ethanol. Each guinea pig will be dosed with the four different concentrations, at four different sites (one concentration/site), two on either side of the spinal column. The appropriate concentration will be applied to a 2x2 cm piece of filter paper to saturation (volume will be recorded) placed directly on the test site. The animals will then be wrapped with plastic sheeting secured with elastic adhesive bandages. The patch(s) will be removed after 24 hours. Observations for signs of dermal irritation will be recorded approximately 24 and 48 hours after removal of the patch. At each observation, all treated sites will be scored for erythema, edema and eschar formation using the scoring system in Appendix B.

If significant irritation (erythema score of greater than 1) is observed at the lowest concentration, additional studies similar to that described above will be performed with lower concentrations.

2. Intradermal:

In order to evaluate the intradermal effects of the test material, two animals will be subjected to preliminary studies as follows:

Animals will be closely clipped over the back with an electric clipper. Each guinea pig will receive test material at two sites[1], one on either side of the spinal column. Both sites will receive 0.1 ml of a 5% solution of the test material via intradermal injection using a syringe fitted with a 25 or 26g 5/8 inch needle. The vehicle commonly used is propylene glycol.

Observations for presence and extent of necrosis will be performed approximately 24 and 48 hours after application. Local necrosis without signs of systemic toxicity will be considered indicative that a 5% concentration will be tolerated.

If extensive necrosis or toxic effects occur, additional studies similar to that described above will be performed with a lower concentration.

Results of the range-finding study will be discussed with the sponsor prior to initiation of the main study.

---

[1]Additional sites may be used for other test materials and/or concentrations. Each animal can have up to twelve sites.

~~17 of 18~~
18-649x)

6837-86

APPENDIX C

No reaction ---------- 0

Very slight (barely perceptible) erythema, usually nonconfluent--------- ±

Slight erythema, usually confluent---------- 1

Moderate erythema---------- 2

Severe erythema, with or without edema, necrosis, or eschar formation--- 3

If edema, necrosis or eschar formation occur, they will also be indicated using the following code:

Edema ------ Ed
Necrosis --- N
Eschar ----- E

~~18 of 18~~
19 6497

6837-86

APPENDIX D

ALLERGENICITY RATING

Sensitization Rate (%)	Grade	Classification
0 - 8	I	Weak
9 - 28	II	Mild
29 - 64	III	Moderate
65 - 80	IV	Strong
81 - 100	V	Extreme

REPORT APPENDIX C

LETTERS OF AUTHORIZATION

BIO/DYNAMICS PROJECT NO.: 6837-86

FINAL REPORT FOR:

GUINEA PIG MAXIMIZATION TEST WITH PX 073086 (025-86B)

C-1
6837-86

15-64930

Allied Corporation
Department of Toxicology
P.O. Box 1021R
Morristown, New Jersey 07960

August 7, 1986

Ms. Donna L. Blaszcak
Manager, Acute Toxicology
Bio/dynamics Inc.
Mettlers Road
P.O. Box 43
East Millstone, N.J. 08873

Dear Donna,

Please consider this authorization, under existing contract between Allied-Signal Inc. and Bio/dynamics Inc., to conduct a Guinea Pig Maximization Test on test sample PX 073086 (025-868). A Test and/or Control Material Handling Information form (Appendix A) for this sample is enclosed. The sample of PX 073086 (025-868) has been received by the Department of Toxicology, Allied-Signal Inc. and will be delivered to Bio/dynamics within one to two weeks from the date of this authorization.

Sponsor Project Number MA-148C and Protocol Number 86057 are to be used to identify this study in all future correspondence.

Based on a Bio/dynamics price list dated April, 1986 (prices subject to confirmation upon receipt of final protocols and study designs), the cost of this study is approximately $5,000 (including a positive control material) and is $3,000 if tested as an additional material using a single common positive control group.

Please inform me of the start, finish and estimated report dates as soon as this study is scheduled.

Sincerely yours,

Brendan J. Dunn

Brendan J. Dunn, M.S.
Senior Toxicologist
Department of Toxicology

BJD:rb
Enc.

cc: G. Loewengart
A.M. Picone
G.A. Roy
G.M. Rusch
File

6837-86
DIST: 8/11/86
CSA
DCB
SET-2
KHK
US

C-2

Allied Corporation
Department of Toxicology
P.O. Box 1021R
Morristown, New Jersey 07960

October 16, 1986

Ms. Donna L. Blaszcak
Manager, Acute Toxicology
Bio/dynamics, Inc.
Mettlers Road, P.O. Box 43
East Millstone, N.J. 08873

Dear Donna,

Regarding our phone conversation on October 15, 1986, below please find information regarding choice of vehicle and selection of dose concentrations for a dermal irritation range-finding test of PX 073086 (025-86B) in guinea pigs. This range-finding test should provide irritation data that will help select dose concentrations for the Guinea Pig Maximization Test (GPMT) of PX 073086 (Sponsor Project MA-148C and Protocol No. 86057). In addition, the vehicle and dose concentrations are outlined for the concurrent GPMT of the standard positive control material, DNCB.

Range-finding Test of PX 073086 (025-86B)

- Vehicle: distilled water (DW)
- id Injection Concentrations: 1,3,5% (v/v) in DW and in FCA emulsion
  Volume/id Injection: 0.1 mL
- Topical Patch (24 h) Concentrations: 10,25,50, (v/v) in DW and neat
  Volume/patch: 0.5 mL

GPMT of DNCB

- Vehicle: propylene glycol (PG) for induction and challenge
- id Injection on Day 0: 0.1% (w/v), emulsify in PG and in FCA emulsion
- Topical Patch (48 h) on Day 7: 0.1% (w/v), emulsify in PG
- Challenge on Day 21: 0.1% (w/v), emulsify in PG

If you have any questions concerning this information, I will be glad to answer them. Please call as soon as you have range-finding test results for PX 073086, so that we can select appropriate dose concentrations for the GPMT.

Sincerely yours,

Brendan

Brendan J. Dunn, M.S.
Senior Toxicologist

BJD:rb

cc: G. Loewengart
G.A. Roy
G.M. Rusch
File

P.I.S.T. 10/22/86
DLB
JET-2

Proj # 6837-86

REPORT APPENDIX D

COMPLIANCE STATEMENT

BIO/DYNAMICS PROJECT NO.: 6837-86

FINAL REPORT FOR:

GUINEA PIG MAXIMIZATION TEST WITH PX 073086 (025-86B)

Compliance Statement

To the best of our knowledge, the study (Bio/dynamics Project No.: 6837-86) was conducted in general conformance with the Environmental Protection Agency TSCA Good Laboratory Practice Standards, 40 CFR 792 with the following exception:

Test substance characterization and stability data remains the responsibility of the sponsor. Assay to verify concentration, stability and homogeneity of the test substance in the carrier were not performed.

These deviations should not affect the results or conclusions of the study.

Donna L. Blaszcak 11/4/87

Donna L. Blaszcak, B.S., AALAS R.L.A.T. Date
Study Director
Manager, Acute Toxicology

REPORT APPENDIX E

QUALITY ASSURANCE STATEMENT

BIO/DYNAMICS PROJECT NO.: 6837-86

FINAL REPORT FOR:

GUINEA PIG MAXIMIZATION TEST WITH PX 073086 (025-86B)

Appendix E

Quality Assurance Statement

Listed below are dates that this study was inspected by the Quality Assurance Unit of Bio/dynamics, Inc. and the dates findings were reported to the Study Director and Management.

Date(s) of Inspection	Reported to Study Director	Reported to Management
11/4/86	11/11/86	11/11/86
11/5/86	12/29/86	12/30/86 and 12/31/86
6/13/87 to 6/20/87	6/24/87 and 8/6/87	8/10/87 and 8/20/87

Florence S. Gilson

Florence S. Gilson, B.S., AALAS L.A.T.
Supervisor of Quality Assurance

November 5, 1987
Date

ALLIED
Morris Township, New J
MA-RR-87-1203

Date: NOVEMBER 23,1987

To: H.C. FOGLE

From: G. LOEWENGART

Subject: **TRANSMITTAL OF FINAL REPORT**
WATER TREATMENT CHEMICALS
MA-148C

Guinea Pig Maximization Test With PX 073086 (025-86B)
Report No. MA-148-80-22

Enclosed is one copy of the subject report. This test was a repeat of a previously conducted sensitization test to determine if the reduced concentration of monomers in PX 073086, as compared to an earlier formulation represented by test material PX 011085, changed the skin sensitization potential of this water treatment polymer formulation.

Four of the fifteen animals (27%) challenged with PX 073086 (025-86B) fourteen days after induction, exhibited clear dermal responses at challenge. A second challenge was performed seven days after the first challenge. Eleven of the fifteen animals (73%) re-challenged exhibited positive responses. No significant dermal responses occurred in irritation control animals at challenge or re-challenge. Therefore, under conditions of this study, PX 073086 (025-86B) exhibited a potential to produce dermal sensitization in the guinea pig and is categorized as a strong (Grade IV) sensitizer.

Results of this GPMT of PX 073086 (025-86B) are very similar to those reported for test material PX 011085 (8361-64) on February 28, 1985 (Report MA-148-80-5 entitled "Guinea Pig Maximization Test of PX 011085"). At least three of fifteen animals (20%) challenged with PX 011085 showed positive dermal responses and after a second challenge application one week later, eleven of fifteen animals (73%) exhibited dermal responses indicative of sensitization. PX 011085 was also classified a Strong Sensitizer (Grade IV)

Please call if you have any questions related to the test results.

GL - 3389

/rb
Attachment

cc: D.J. Billmaier, M.D.*
J.B. Charm*
E.J. Freeman*
L.R. Gelosa*
J.A. Hathaway, M.D*
R. Highsmith
R. Jobbins*
D. Levine
R.W. Reinhold*
G.A. Roy - Archives
G.M. Rusch*
T.N. Stewart*
I.S. Library
File

Triage of 8(e) Submissions

Date sent to triage: 2/5/96

NON-CAP CAP

Submission number: 12216 A

TSCA Inventory: Y N D

Study type (circle appropriate):

Group 1 - Dick Clements (1 copy total)

ECO AQUATO

Group 2 - Ernie Falke (1 copy total)

ATOX SBTOX SEN w/NEUR

Group 3 - Elizabeth Margosches (1 copy each)

STOX CTOX EPI RTOX GTOX

STOX/ONCO CTOX/ONCO IMMUNO CYTO NEUR

Other (FATE, EXPO, MET, etc.): _____

Notes:

THIS IS THE ORIGINAL 8(e) SUBMISSION; PLEASE REFILE AFTER TRIAGE DATABASE ENTRY

For Contractor Use Only

entire document: 0 1 2 **pages** 1,2 **pages** 1/2, tabs

Notes:

Contractor reviewer : LPS **Date:** 5/11/95

CECATS\TRIAGE TRACKING DBASE ENTRY FORM

CECATS DATA:
Submission # 8EHQ- 1092 -12216 SEQ. A

TYPE: (INT.) SUPP FLWP

SUBMITTER NAME: Rhone - Poulenc Inc.

INFORMATION REQUESTED: FLWP DATE:
0501 NO INFO REQUESTED
0502 INFO REQUESTED (TECH)
0503 INFO REQUESTED (VOL ACTIONS)
0504 INFO REQUESTED (REPORTING RATIONALE)

DISPOSITION:
(0639) REFER TO CHEMICAL SCREENING
(0678) CAP NOTICE

VOLUNTARY ACTIONS:
(0401) NO ACTION REPORTED
0402 STUDIES PLANNED/UNDERWAY
0403 NOTIFICATION OF WORKERS
0404 LABEL/MSDS CHANGES
0405 PROCESS/HANDLING CHANGES
0406 APP./USE DISCONTINUED
0407 PRODUCTION DISCONTINUED
0408 CONFIDENTIAL

SUB. DATE: 10/29/92 OTS DATE: 10/29/92 CSRAD DATE: 04/04/95

CHEMICAL NAME: | CAS#

Px 073086 Px Solution Polymer | none
1-propanaminium, 2-hydroxy-N,N,N-trimethyl- | Unknown
3-[(2-methyl-1-oxo-2-propenyl)oxy]-nitrate(salt), polymer
with 2-propenamide and 2-propenoic acid | 79-06-1
79-10-7

INFORMATION TYPE:		P F C	INFORMATION TYPE:		P F C	INFORMATION TYPE:		P F C
0201	ONCO (HUMAN)	01 02 04	0216	EPI/CLIN	01 02 04	0241	IMMUNO (ANIMAL)	01 02 04
0202	ONCO (ANIMAL)	01 02 04	0217	HUMAN EXPOS (PROD CONTAM)	01 02 04	0242	IMMUNO (HUMAN)	01 02 04
0203	CELL TRANS (IN VITRO)	01 02 04	0218	HUMAN EXPOS (ACCIDENTAL)	01 02 04	(0243)	CHEM/PHYS PROP	01 02 04
0204	MUTA (IN VITRO)	01 02 04	0219	HUMAN EXPOS (MONITORING)	01 02 04	0244	CLASTO (IN VITRO)	01 02 04
0205	MUTA (IN VIVO)	01 02 04	0220	ECO/AQUA TOX	01 02 04	0245	CLASTO (ANIMAL)	01 02 04
0206	REPRO/TERATO (HUMAN)	01 02 04	0221	ENV. OCCC/REL/FATE	01 02 04	0246	CLASTO (HUMAN)	01 02 04
0207	REPRO/TERATO (ANIMAL)	01 02 04	0222	EMER INCI OF ENV CONTAM	01 02 04	0247	DNA DAM/REPAIR	01 02 04
0208	NEURO (HUMAN)	01 02 04	0223	RESPONSE REQEST DELAY	01 02 04	0248	PROD/USE/PROC	01 02 04
0209	NEURO (ANIMAL)	01 02 04	(0224)	PROD/COMP/CHEM ID	01 02 04	0251	MSDS	01 02 04
0210	ACUTE TOX. (HUMAN)	01 02 04	0225	REPORTING RATIONALE	01 02 04	0299	OTHER	01 02 04
0211	CHR. TOX. (HUMAN)	01 02 04	0226	CONFIDENTIAL	01 02 04			
0212	ACUTE TOX. (ANIMAL)	01 02 04	0227	ALLERG (HUMAN)	01 02 04			
0213	SUB ACUTE TOX (ANIMAL)	01 02 04	(0228)	ALLERG (ANIMAL)	01 02 04			
0214	SUB CHRONIC TOX (ANIMAL)	01 02 04	0239	METAB/PHARMACO (ANIMAL)	01 02 04			
0215	CHRONIC TOX (ANIMAL)	01 02 04	0240	METAB/PHARMACO (HUMAN)	01 02 04			

TRIAGE DATA:

NON-CBI INVENTORY
(YES)
NO
(DETERMINE)

ONGOING REVIEW
YES (DROP/REFER)
NO (CONTINUE)
REFER:

SPECIES
GP

TOXICOLOGICAL CONCERN:
LOW
(MED)
(HIGH) Dermal Sensitization

USE:

PRODUCTION:

COMMENTS:

#12216A

Dermal sensitization is of ~~high~~ medium concern based on dermal responses in 11/15 guinea pigs at re-challenge utilizing the Magnusson and Kligman maximization test. At the first challenge, 4/15 guinea pigs exhibited a dermal response.